

Research Title: " Prevention of pre-eclampsia using metformin: a randomized control trial (PREMET)"

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RESEARCH CONSENT FORM



1. Title of research

Prevention of pre-eclampsia using metformin: a randomized control trial (PREMET)

2. Principal Investigator

Mahmoud Mohamed, Women Wellness and Research Center, Doha, Qatar

3. Why are we inviting you to join this research?

The investigator and colleagues at Hamad Medical Corporation (HMC) and Sidra Medicine are conducting this research.

We are inviting you to join this research because you are at high risk of developing pre-eclampsia (PET) based on your history and current status. You become at high risk because you have one of the following; maternal age, obesity, medical disorders that might increase PET risk such as antiphospholipid syndrome, hypertensive disorders, renal diseases, diabetes mellitus or previous PET. It is known that, PET causes numerous maternal and neonatal complications and there is no effective preventive or treatment modality known except delivery.

4. What should you know about this research?

- We will explain the research to you
- Whether or not you join is your decision (you can accept or refuse no matter who is inviting you to participate)
- Please feel free to ask questions or mention concerns before deciding, or during or after the research
- You can say yes but change your mind later
- We will not hold your decision against you

5. Who can you talk to?

If you have questions or concerns, or if you think the research has hurt you, talk to the research team at: Mr. Mahmoud Mohamed, Dr. Mariam Kunjachen, Dr. Racheal Lobo, Dr. Manal Shakir, Dr. Lamis Alsayed
If you have questions about your rights as a volunteer, or you want to talk to someone outside the research team, please contact:

- HMC Institutional Review Board (HMC-IRB) Chair at 5554 6316
- HMC-IRB Office at 4025 6410 (from Sunday to Thursday between 7:00am-3:00pm) or email at irb@hamad.qa

6. Why are we doing the research?

In the prevalence of PET and its risk factors is high. To date, there is no effective treatment for PET except developed PET, you doctor might need to deliver you early than expected which might result in giving premature infant. In this study we are aiming to prevent you from developing PET by administering



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metformin. Metformin is known for its high safety profile in pregnancy. It is used in treatment of gestational and type 2 diabetes during pregnancy for decades. There is no expected harm on your developing baby or your health. In contrast it has been found to improve pregnancy outcomes. Previous studies found that women who used metformin for treatment of diabetes are less likely to develop PET compared to women who used insulin. Therefore, metformin is believed to be effective in prevention of PET.

In addition to that, we will be taking 5 ml blood sample with your routine blood investigation to study a new available biomarker and determine molecular mechanism associated with PET. The blood test for the new biomarker is proven to help predict your likelihood of developing PET in the near future (next two weeks), which will help you doctor plan your care accordingly.

Your blood and tissue samples contain genes (DNA) that serve as the "instruction book" for your body. Your samples and medical information will help us study how genes influence PET.

7. How long will the research take?

We think that you will be in the research for a maximum period up to 11 months.

We expect the research to last for 2 years.

8. How many people will take part?

We plan to study 414 women at Women Wellness and Research Center.

9. What happens if you take part?

Taking part in this research will entail the following:

- Attending the Women Wellness and Research Center on three occasions each of which will last for approximately 30 minutes. These visits will be timed to coincide with your antenatal appointments wherever possible so as to minimize you making additional visits to the hospital
- Giving 5 ml (a teaspoonful) of blood in addition to your routine blood investigation (3 times). Again, we will make every effort to collect this very small amount of blood when you have your routine blood test in pregnancy. If you are admitted into the hospital for any complication related to high blood pressure or are delivering early, an additional tiny amount of blood (5ml or one teaspoonful) will be collected.
- Answering questions about your medical history
- Taking study medicines (specifically aspirin and/or metformin). You would be expected to return any unused medicines for the purpose of audit and monitoring of the study. The metformin we are using here has been shown to decrease a woman's chances of developing a high blood pressure and its complications such as what is known as pre-eclampsia or PET (high blood pressure and protein in urine). This medicine is safe in pregnancy
- Us calling you (at most three times) between visits to check up on your health and answer any questions. These phone calls (**maximum of 3 telephone calls**) will normally be very short lasting for a maximum of 3-5 minutes.
- Allowing us to take a small portion (sample) of the afterbirth (placenta) for genetic testing

You will be "assigned (randomized)" into one of two groups (the intervention and control groups) study groups blindly (i.e. neither you nor the person assigning you will know which group you will be assigned).



The intervention group will be for those who in addition to standard antenatal care and aspirin 100 mg once daily will also be taking metformin 1 gm twice daily until delivery.

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- The Control group will be for those receiving standard care and aspirin 100 mg once daily only.

Randomization means that you will be assigned into a group by chance. It is like flipping a coin. Neither you nor the researchers choose which group you will be in. You will have a 50% chance of being placed in a specific group.

10. Could the research be bad for you?

- Although metformin is a safe medication, you might experience mild nausea, vomiting, abdominal pain, diarrhea and headache and rarely low sugar levels. Most of these side effects tend to settle once your body gets used to the medicine. However, you will be monitored, for early identification of these side effects and management of them. We would like to reassure you that these side effects are rare and furthermore there are no recognizable clearly increased risk to either your baby or yourself.

There are also some privacy risks that are unlikely, but that you should know about:

- Although your genetic information is unique to you, you share some genetic information with blood relatives. Genetic information from them could therefore be used to help identify you. Genetic information from you could also be used to help identify them.
- Although we will protect your information (see Section 12), people may develop ways in the future to link your genetic or medical information in our databases back to you. For example, someone could compare information in our databases with information from you (or a blood relative) in another database and be able to identify you (or your blood relative). It also is possible that there could be violations to the security of the computer systems used to store the codes linking your genetic and medical information to you.
- Since some genetic variations can help to predict future health problems, this information might be of interest to health providers, life insurance companies, and others. Law enforcement agencies can also use genetic variations to identify a person or his/her blood relatives. Therefore, your genetic information potentially could be used in ways that could cause you or your family distress, such as by revealing that you (or a blood relative) carry a genetic disease.
- It is possible that study findings could one day help people of the same race, ethnicity or sex as you. But it is also possible that genetic traits might become associated with your group and might reinforce harmful stereotypes.
- There also may be other privacy risks that we have not foreseen.

11. Could the research be good for you?

We cannot promise any benefit to you or to others from you joining this research. However, possible benefits include helping science to find a new prevention for PET. If the intervention is proven to be effective this can help all pregnant women at risk of developing this complication in pregnancies.

This kind of research usually takes a long time to produce medically useful results, so we will not report genetic test results to you or your doctor.

12. What happens to information about you?

We will make efforts to secure information about you. This includes using a code to identify you in our records instead of your name. We will not identify you personally in any reports or publications about this research.

We will guarantee complete secrecy, but we will limit access to information about you. Only people who have a



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need to review information will have access. These people might include:

- Members of the research team and other Data Safety Monitoring Committee representatives whose work is related to the research or to protecting your rights and safety
- Representatives of the Ministry of Public Health Qatar who make sure the study is done properly and that your rights and safety are protected
- Your doctors and nurses

Also, your specimen will be analyzed in HMC pathology department and at Sidra Medicine.

During the study, your samples will be kept and used in Qatar only. We would like to keep any samples left over at the end of the study for 2 years for future research.

We will store these leftover samples without a link to your identity. Leftover samples will be used by the study team and might be shared with researchers who were not part of this study. Your leftover samples will be used for research into any condition. This research might include genetic research.

You can change your mind and withdraw your samples from the study by contacting us before Jul 2020. After that, we will not know which samples belong to you and we will not be able to remove them from the study.

You may join this study even if you do not allow this future use. You can mark your choice at the end of this form. If you do not allow storage of your samples, we will destroy the sample within two years after the end of the study.

We plan to use data from this study in other projects in the future. This might include sharing the data with other researchers. Before we store the data for future use, we will destroy all links between your identity and the data about you.

Information from analyses of your samples and medical information will be put into databases along with information from other volunteers. This will help researchers around the world.

These databases will not include your name, telephone number or other information that directly identifies you.

13. What if you don't want to join?

You can say no and we will not hold it against you.

14. What if you join but change your mind?

You can stop participating at any time and we will not hold it against you.

We will tell you about any new information that might affect your health or welfare, or might affect your willingness to continue in the research.

If you stop participating, we will ask you for permission to collect information from your medical record.

If you stop participating, we cannot delete information and samples that we have already collected about you.

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should you know?

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This research is funded by Medical Research Center, Hamad Medical Corporation.

If you are injured as a direct result of research procedures, contact the investigator and appropriate care will be made available at HMC. If you seek care outside of HMC, such care will be at your expense. Compensation is not available in case of injury.

The investigator or sponsor may stop the study or take you out of the study at any time, even if you would like to continue. This could happen because breach of the protocol.

Your specimens might help in the development of commercial products, such as new treatments or diagnostic tests. You will not receive any financial compensation for commercial products.

16. Additional Choices

In Section 12, we explained that we would like to use your samples for future research. Please indicate your choice by initialing the appropriate line below:

_____ I **ALLOW** storage and use of my samples for future research.

_____ I **DO NOT ALLOW** storage or use of my samples for future research.



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Signature Page for Capable Adult

Volunteer

I voluntarily agree to join the research described in this form.

Printed Name of Volunteer

Signature of Volunteer Date

Person Obtaining Consent

I document that:

- *I (or another member of the research team) have fully explained this research to the volunteer.*
- *I have personally evaluated the volunteer's understanding of the research and obtained their voluntary agreement.*

Printed Name of Person Obtaining Consent

Signature of Person
Obtaining Consent Date

Witness (if applicable)

I document that the information in this form (and any other written information) was accurately explained to the volunteer, who appears to have understood and freely given Consent to join the research.

Printed Name of Witness

Signature of Witness Date

